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14. ABSTRACT
This document explains the change in Principal Investigator for the award as of 13 Jul 2009. The initial Principal Investigator has relocated to another institution, and has relinquished the award back to Cleveland Clinic. Subsequent conversations with TATRC have led to a new project focus, utilizing deep brain stimulation (DBS) for the treatment of traumatic brain injury-related epilepsy. The new Principal Investigator, Dr. Imad Najm, is in the process of finalizing his protocol and obtaining final institution approval to commence the study.

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Introduction

This award (W81XWH-08-2-0211) was initially focused on investigating the use of deep brain stimulation (DBS) on traumatic brain injured patients in a minimally conscious state. However in July of 2009, the initial Principal Investigator left the institution for another position. The individual ceded the award back to Cleveland Clinic.

At that time, Cleveland Clinic (with approval of the Telemedicine & Advanced Technology Research Center) decided to alter the focus of the award to take better advantage of the unique resources and capabilities at Cleveland Clinic to focus on the application of deep brain stimulation (DBS) for the treatment of post-traumatic brain injury (TBI) epilepsy.

One of the aforementioned resources at Cleveland Clinic is our Epilepsy Center. Cleveland Clinic has one of the largest and most comprehensive programs in the world for the evaluation and medical and surgical treatment of epilepsy in children and adults.

The Epilepsy Center was established at the Cleveland Clinic to meet the unique needs of patients with pediatric and adult epilepsy. Very few medical centers in the United States, and in the world, provide the range of care that is available here.

Our project melds the talents of the epileptologists and clinical neurophysiologists within the Epilepsy Center with the DBS expertise located in the Clinic's Center for Neurological Restoration. The intellectual and physical resources found within these two centers will be brought to bear on epilepsy, a condition which has been shown to develop in an increased frequency for individuals having suffered a TBI.

The goal of our highly multidisciplinary and translational proposal is to detect surrogate markers of potentially epileptogenic regions non-invasively (through neurophysiologic/EEG and imaging/MRI studies), prevent epileptogenesis, and control epilepsy by selectively applying electrical stimulation (ES) of brain structures directly involved in the generation and/or spread of paroxysmal activity. Based on the results of the animal studies, we will design a pilot clinical study using chronic low frequency deep brain electrical stimulation of the thalamus on a small number of patients with non-surgically remediable medically intractable epilepsy secondary to traumatic brain injury.

We will accomplish our goals through the use of our unique and highly multidisciplinary translational resources within the Neurological Institute (Epilepsy Center, Center for Neurological Restoration, and Neuroimaging Center). Specifically, we plan to accomplish the following in a rat model of TBI and patients with TBI-induced medically intractable epilepsy:

Aim 1: To study the imaging (MRI) and acute/subacute electroencephalographic (EEG) changes following TBI in the rat and assess the predictive value of the changes in the later development of epilepsy (imaging and neurophysiological surrogates of epileptogenesis)

Aim 2: To test the effect of continuous, chronic stimulation (LFS and HFS) of the central thalamus on FPI-induced epileptogenesis in the rat. We hypothesize that continuous LFS of the central thalamus will prevent the development of FPI-induced epileptogenesis through its

neuromodulatory effect on its cortical target areas (in particular the frontal cortical regions which are the most affected by TBI), and will prevent the later recurrence of spontaneous seizures in animals after they develop spontaneous seizures (neuromodulatory effect of the DBS on epileptogenesis following TBI).

Aim 3: To test the effect of thalamic chronic electrical stimulation on TBI-induced seizures in the rat. Because we have recently shown that thalamic stimulation alone significantly reduces seizure severity in a model of generalized seizures, we hypothesize that thalamic stimulation will suppress seizures following TBI (antiepileptic effect of DBS following TBI).

Aim 4: To design a pilot study to assess the effect of DBS on a small group of patients who suffer from medically intractable epilepsy following TBI.

To date, no funds have been expended on research for either the previous project or the final project concept focusing on epilepsy. We are now in the process of finalizing our protocol and obtaining final institutional approval. We anticipate beginning our study no later than the first quarter of 2010, and for the data acquisition portion of the study to occur within 24 months.